1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

TERTROXIN 20 µg tablets

2. QUALITATIVE AND QUANTITATIVE

Each tablet of TERTROXIN 20 µg contains 20 µg liothyronine sodium.

Contains sugar: Lactose 48,5 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

TERTROXIN 20 µg is a white, uncoated biconvex tablet with breakline and embossed with "TERTROXIN" and "GLAXO".

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

TERTROXIN 20 µg is indicated in the treatment of:

- coma due to myxoedema;
- management of severe chronic thyroid deficiency;
- hypothyroid states arising in treatment of thyrotoxicosis;

- TERTROXIN 20 µg is also used therapeutically in thyrotoxicosis as an adjunct to carbimazole.

After six months of this treatment it may be possible to distinguish drug-responsive patients from relapse-prone patients who are better treated with radio-iodine or surgery. Large doses of liothyronine normally suppress the uptake of iodine by the thyroid, but not in thyrotoxicosis and this forms the basis of a routine test for thyrotoxicosis.

4.2. Posology and method of administration

Posology

Adults

Thyroid deficiency:

Treatment of adults may be started with doses of 10 µg to 20 µg increasing gradually to a total daily dosage of 80 µg to 100 µg after a few days.

Myxoedema coma:

100 µg or more may be administered by stomach tube.

Thyrotoxicosis:

As a diagnostic test in adults, 80 µg or more of liothyronine are given daily for seven or eight days. The daily amount should be divided into 3 or 4 doses. Radio-iodine is then administered, and uptake by the thyroid can be estimated about 20 minutes later. Failure to suppress the uptake of radio-iodine is indicative of thyrotoxicosis.

As therapy for thyrotoxicosis with carbimazole:

In adults 80 µg of liothyronine daily. In some patients it is possible to discontinue the carbimazole after about a year without subsequent relapse.

Elderly population

The initial dosage should be 5 µg daily (see Method of administration below to obtain small doses). TERTROXIN 20 µg should be given in divided doses two or three times daily.

Paediatric population

The initial dosage should be 5 µg daily (see Method of administration below to obtain small doses). TERTROXIN 20 µg should be given in divided doses two or three times daily.

Method of administration

For oral administration.

To obtain small doses:

To obtain small doses tablets may be crushed and triturated with lactose for administration as a powder (see Elderly population and Paediatric population above).

4.3. Contraindications

TERTROXIN 20 µg is contraindicated in:

- Patients with hypersensitivity to liothyronine sodium or to any excipients in TERTROXIN 20 µg (see section 6.1).
- Patients with angina of effort or cardiovascular disorders.
- Patients with untreated adrenal cortical insufficiency.
- Patients with untreated hyperthyroidism.

4.4. Special warnings and precautions for use

Endocrine Disorders

TERTROXIN should be used with caution in patients with concomitant endocrine diseases such as diabetes mellitus or adrenocortical insufficiency.

Myxoedema and myxoedemic coma

In myxoedema, care must be taken to avoid imposing excessive burden on cardiac muscle affected by prolonged severe thyroid depletion. Glucocorticoids should be used in conjunction with thyroid hormones in the management of myxoedemic coma.

Cardiovascular disorders and angina

Angina may be precipitated where there is latent cardiac ischaemia (see section 4.3).

Hypothyroidism

In severe prolonged hypothyroidism, the decreased level of adrenocortical activity may require supplementation with adrenocorticotrophic hormones. Adrenal deficiency must be corrected in patients with hypopituitarism prior to commencement of liothyronine therapy. The use of thyroid hormones has been reported to precipitate a hyperthyroid state.

Obesity

TERTROXIN 20 µg should not be used in the management of obesity in euthyroid patients because doses within the range of daily hormonal requirements are ineffective and larger doses may produce serious or life-threatening adverse effects.

Antidiabetic medicines and anticoagulants

Thyroid treatment may enhance the action of anticoagulants, requiring an initial increased frequency of monitoring of prothrombin times and upset the stability of patients receiving

antidiabetic medicines. It is important to remind patients of increased insulin requirements if they are prescribed TERTROXIN 20 µg.

Patients should also be reminded of the importance of reporting to the doctor any chest pain, palpitations or excessive sweating.

Laboratory tests

Periodic assessment of thyroid status should be conducted by means of appropriate laboratory tests and clinical observation.

Elderly population

Special care is needed in the elderly who may exhibit increased sensitivity to the effects of thyroid replacement therapy (see section 4.2).

Paediatric population

Infants

Craniosynostosis may occur in infants given high doses of thyroid hormones (see section 4.2).

Children

A partial loss of hair may occur in children (paediatric patients) that are administered with thyroid hormones in the first few months of thyroid therapy, however this effect is usually a transient phenomenon, and later recovery is usually the rule (see section 4.2).

Excipients

TETROXIN 20 µg contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take

TERTROXIN 20 µg.

4.5. Interaction with other medicines and other forms of interaction

Anticoagulants

TERTROXIN 20 µg therapy may potentiate the action of anticoagulants by increasing the catabolism of Vitamin K dependent clotting factors.

Anticonvulsant

Initiation or discontinuation of anticonvulsant medicines may alter liothyronine dose requirements. The effect of thyroid preparations, such as TERTROXIN 20 µg, may be enhanced by phenytoin taken concomitantly. Phenytoin levels may be increased by liothyronine. Anticonvulsants such as carbamazepine and phenytoin enhance the metabolism of thyroid hormones and may displace them from plasma proteins.

Aspirin

The effect of thyroid preparations may be enhanced by aspirin. Aspirin displaces thyroid hormones from protein-binding sites.

Ketamine

Ketamine may cause hypertension and tachycardia when administered to patients receiving thyroid replacement therapy.

Oral contraceptives

Co-administration of oral contraceptives may result in an increased dosage requirement of thyroid therapy as estrogens increase levels of thyroid binding globulin.

Cardiac glycosides

If co-administered with cardiac glycosides, adjustment of the dosage of cardiac glycoside

may be necessary. Thyroxine may potentiate digitalis toxicity. The increased metabolic rate following liothyronine therapy may increase digitalis requirements.

Colestyramine

Colestyramine given concurrently reduces gastrointestinal absorption of liothyronine as contained in TERTROXIN 20 µg, by binding liothyronine within the gut lumen.

Tricyclic antidepressants

TERTROXIN 20 µg increases receptor sensitivity to catecholamines thus potentially increasing the risk of cardiac dysrhythmias in patients receiving tricyclic antidepressants.

Monitoring patients on liothyronine therapy

A number of medicines may affect thyroid function tests and this should be borne in mind when monitoring patients on liothyronine therapy.

Insulin / oral hypoglycaemics

Patient requirements of insulin or oral hypoglycaemics may increase in patients receiving therapy with liothyronine.

4.6. Fertility, pregnancy and lactation

Pregnancy

There is limited placental transfer of thyroid hormones.

Breastfeeding

Liothyronine, as contained in TERTROXIN 20 µg, is excreted in breast milk.

Fertility

No data available.

4.7. Effects on ability to drive and use machines

Since adverse reactions such as headaches have been reported in patients receiving TERTROXIN 20 µg, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that TERTROXIN 20 µg does not adversely affect their ability to do so (see section 4.4 and/or 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

At the beginning of treatment, ordinary therapeutic doses may cause anginal pain, palpitations and cramps in the skeletal muscle.

b) Tabulated list of adverse reactions

System organ class	Less Frequent
Endocrine disorders	Myxoedema[2]
Metabolism and nutrition disorders	Excessive loss of weight[1]
Psychiatric disorders	Restlessness[1], excitability[1]
Nervous system disorders	Headache[1]
Cardiac disorders	Cardiac dysrhythmias[1], tachycardia[1]
Vascular disorders	Flushing[1]
Gastrointestinal disorders	Diarrhoea[1]
Skin and subcutaneous tissue disorders	Sweating[1]
Musculoskeletal and connective tissue disorders	Muscle weakness[1]

c) Description of selected adverse reactions

[1]TERTROXIN 20 µg is capable of producing the same side effects and can show the same

symptoms of overdosage as the thyroid hormone, but in practice (except in myxoedema) these symptoms are uncommon and they disappear rapidly when treatment is stopped or the dosage is reduced, also refer to section 4.9. Overdose.

[2]The euthyroid patient shows much greater tolerance to the thyroid hormone than the thyroprivic case. It has already been mentioned that in myxoedema side effects from the rapid re-establishment of the normal state may occur; these too are quickly controlled by reducing the dosage.

Reporting of suspected adverse reactions

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to

SAHPRA: via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088 / +27 (0)11 239-6200

4.9. Overdose

Symptoms

The following effects are indicative of excessive dosage, and usually disappear on reduction of dosage or withdrawal of treatment for a day or two. Anginal pain, cardiac dysrhythmias, palpitation, and cramps in skeletal muscle; also, tachycardia, diarrhoea, restlessness, irritability, nervousness excitability, headache, flushing, sweating, excessive loss of weight and muscular weakness. Congestive heart failure may be induced or aggravated.

Treatment

Dosage should be reduced or therapy temporarily discontinued if signs and symptoms of overdose appear. Treatment may be reinstated at a lower dosage. In normal individuals, normal hypothalamic-pituitary-thyroid axis function is restored in 6 to 8 weeks after thyroid suppression.

Treatment of acute massive thyroid hormone overdosage, is aimed at reducing gastrointestinal absorption of the medicines and counteracting central and peripheral effects, mainly those of increased sympathetic activity. Vomiting may be induced initially, if further gastrointestinal absorption can be reasonably prevented and barring contraindications such as coma, convulsions, or loss of the gagging reflex.

Treatment is symptomatic and supportive.

Oxygen may be administered, and ventilation maintained. Measures to control fever, hypoglycemia, or fluid loss, should be instituted if needed. The patient may present in shock. Symptoms may resemble thyroid storm and treatment is symptomatic. Congestive heart failure may require appropriate treatment. Supportive measures may include measures such as the management of fever, hypoglycaemia or fluid loss if necessary, as per the above.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and class: A 21.3 Thyroid preparation

Pharmacotherapeutic group: Thyroid preparation

ATC code: H03AA02

Mechanism of action

The principal pharmacological effect of exogenous thyroid hormones is to increase the metabolic rate of body tissues.

Liothyronine (l-triiodothyronine) sodium is a naturally occurring thyroid hormone. Its biological action is qualitatively similar to that of thyroxine, but the effect develops in a few hours and disappears within 24 to 48 hours of stopping treatment.

5.2. Pharmacokinetic properties

Absorption

Liothyronine is readily and almost completely absorbed from the gastrointestinal tract following oral administration.

Distribution

In the circulation, liothyronine is principally bound to thyroxine-binding globulin (TBG). The plasma half-life of liothyronine in euthyroidism is approximately 1 to 2 days; it is prolonged in hypothyroidism and reduced in hyperthyroidism.

Biotransformation

Liothyronine is metabolised by deiodination to inactive di-iodothyronine and mono-iodothyronine. Further metabolites result from deamination and decarboxylation to tiratricol (triac).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Acacia powder, lactose, magnesium stearate, maize starch, sodium chloride.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

6.5. Nature and contents of container

50 tablets are packed in an amber vial and sealed with a plastic semi opaque white polyethylene snap cap, together with a white barrel shaped polyurethane foam insert.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

G 3082 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION

Date of registration: Old medicine

10. DATE OF REVISION OF TEXT

02 June 2023

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088

Namibia: NS2 15/21.3/0121

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